REMARKS

Claims 14-37 are pending in the instant application. Claims 14-37 have been rejected. Claims 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 and 36 have been amended. Support for these amendments is provided in the specification at page 3, line 21, through page 4, line 2, page 7, lines 2-12, page 13, line 33, through page 14, line 1, and page 15, lines 24-27. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 14-37 under 35 U.S.C. 112, second paragraph

Claims 14-37 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner suggests that recitation of "native protein" in claims 14-20, 24 and 28-34 is indefinite because it is unclear whether this phrase means the un-denatured form of the protein or a protein that is endogenous to ovarian tissue or cells.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have deleted this phrase from the claims.

Claims 28-37 are also suggested to be indefinite for reciting "A method for binding an ovarian specific native protein on a cell" because the exact meaning of this phrase is not clear.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended this claim to clarify that antibody binds to the protein on the cell. This amendment is consistent with teachings at page 14-15 wherein general, well-known methodologies for in vivo antibody use are set forth.

Further, claim 27 is suggested to be indefinite for reciting "derivative of blood". While Applicants believe that this phrase would be understood by the skilled artisan when read in light of teachings of the specification, in an earnest effort to advance the prosecution of this case, Applicants have deleted this phrase from the claim.

Withdrawal of these rejections under 35 U.S.C. 112, second paragraph is therefore respectfully requested.

II. Rejection of Claims 14-37 under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph

Claims 14-37 have been rejected under 35 U.S.C. 101 as the Examiner suggests that the claimed invention is not supported be either a substantial asserted utility or a well-established utility. Claims 14-37 have also been rejected under 35 U.S.C. 112, first paragraph as the Examiner suggests that one skilled in the art would not know how to use the claimed invention.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that "evidence abounds in which protein levels do not correlate with steady state mRNA levels or alterations in mRNA levels." The literature references relied upon the Examiner to suggest that steady state levels of proteins does not necessarily correlate to steady state levels of mRNA, namely Fu et al. (EMBO Journal 1996 15:4392-4401), Powell et al. Pharmacogenesis, 1998 8:411-421), Vallejo et al. (Biochimie 2000 82:1129-1133) Jang et al. (Clinical and Experimental Metastasis 1997 15:469-483) and Pennica et al. (PNAS 1998 95:14717-14722) are reporting unique findings of scientific interest wherein researchers unexpectedly found that protein and mRNA levels did not always correlate for a unique group of proteins. These references relating to unique proteins, none of which

serve as cancer markers for gynecologic cancers as in the present invention, are hardly representative of the art for proteins in general wherein mRNA levels correlate quite well with protein levels.

Much more relevant are the recent teachings of Lopez-Guerrero et al. (Arkh Patol. 2003 65(1):50-5 (Abstract copy provided herewith via Supplemental IDS) reporting a 93-95% correlation between protein and mRNA levels for the diagnostic breast cancer marker HER-2 detected in the commercially available HercepTest. The commercially available HercepTest, as well as the teachings of Lopez-Guerrero et al., demonstrate the ability of those skilled in the art to extrapolate results such as those disclosed in the instant specification relating to Ovr110 mRNA expression levels to the claimed invention wherein protein levels can also determined. Also more relevant are teachings of Jaakola et al. (Clin Chem. 1995 41(2):177-9), el-Shirbiny et al. (Adv. Clin. Chem. 1994 31:99-133) and Straub et al. (Urology 2001 58(5):815-20) (copies of which are also provided herewith in the Supplemental IDS) showing the correlation between mRNA expression and protein levels of a well known cancer marker, PSA.

Further, Applicants are providing herewith via Supplemental IDS two recent publications which confirm teachings in the instant specification that elevated mRNA

expression of Ovr110 in gynecologic cancer tissues as taught at page 17-24 correlates with measurable protein levels in gynecologic cancers. In particular, Applicants are providing herewith via Supplemental IDS a reference by Tringler et al. published in the March 1, 2005 issue of Clinical Cancer Research which discloses results from a study designed to investigate the expression of the DDO110 protein, also known as Ovr110, which is homologous to B7-H4 (see page 1842, col. 2 of Tringler et al.), in normal breast and in primary and metastatic breast carcinoma. Ovr110 protein exhibited nearly ubiquitous expression in breast cancer, independent of tumor grade or stage and is suggested to have a critical role in breast cancer biology. As taught at page 1842, col. 2, this gynecologic cancer marker was initially identified and characterized via quantitative PCR analysis (such as set forth in the instant specification at pages 17-24). Experiments and results set forth at pages 1843-1845 of Tringler confirm the substantial asserted utility of an antibody of the claimed invention in detecting overexpression of Ovr110 in cancer tissues in accordance with methods such as taught at page 11-15 of the instant specification.

Applicants are also providing via Supplemental IDS herewith a publication by Salceda et al. from Experimental Cell Research which was available publicly online on March

9, 2005 and which will appear in the May 15, 2005 issue of Experimental Cell Research, Volume 306, number 1 at pages 128-141. This paper discloses results from Western blot and IHC experiments with an anti-Ovr110 antibody. In the results section at page 5 of the online publication it is taught that the detection of Ovr110 protein (referred to therein as B7-H4 or DDO110)) "in human breast and ovarian cancers but not in most normal adult tissues by Western blot is in good agreement with mRNA expression data." The Examiner is also respectfully directed to the discussion at page 12 of the online publication wherein it is taught that "B7-H4 mRNA was overexpressed in serous ovarian cancer and a majority of breast cancers with little or no expression in a variety of normal tissues surveyed" and that "Western blots with a monoclonal antibody against B7-H4 showed that B7-H4 protein expression reflected this mRNA distribution".

MPEP § 2164.04 states:

> a specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

The instant specification provides detailed teachings for use of antibodies in diagnostic and treatment methods for cancer at pages 14-15. Detailed antibody assay techniques for detecting Ovr110 are also set forth in the specification at pages 11 through 14. In addition, detectable elevated levels of Ovr110 in gynecologic cancers are demonstrated by the data presented in the specification at pages 17-24. Further, art much more relevant to the instant claimed invention than that cited by the Examiner is supportive of the fact that polynucleotide levels of this cancer marker would be expected to correlate with protein levels and in fact do correlate with protein levels. Accordingly, the claimed antibodies clearly have a substantial asserted utility and there is no reasonable basis to question the teachings of the instant specification regarding this utility.

Thus, the instant specification and claims meet the utility requirements of 35 U.S.C. 101 and the enablement requirements of 35 U.S.C. § 112, first paragraph. Withdrawal of these rejections is therefore respectfully requested.

III. Rejection of Claims 14-37 under 35 U.S.C. 112, first paragraph - Written Description

Claims 14-37 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. In particular, the Examiner suggests that the specification does not have written description for just any gene comprising SEQ ID NO:10-13 and 16, except in the context of SEQ ID NO:1. Further, the Examiner suggests that the specification, while disclosing SEQ ID NO:1 and partial sequences or fragment of SEQ ID NO:1 as 10-13 and 16, does not indicate regions of the sequences that would normally be associated with "genes".

Accordingly, in an earnest effort to advance the prosecution, but without conceding in any way to the correctness of the Examiner's suggestions, Applicants have amended the claims to remove any reference to the term "gene". Instead, claims are drawn to an isolated antibody or antibody fragment that binds specifically to a protein encoded by polynucleotide sequences of any of SEQ ID NO: 1, 10, 11, 12, 13 or 16 in accordance with teachings at page 3, line 21, through page 4, line 2, page 7, lines 2-12 and page 15, lines 24-27.

Applicants were clearly in possession of the polynucleotide sequences as set forth in the claims and

thus, this amendment overcomes any written description rejection.

Withdrawal of these rejections under 35 U.S.C. 112, first paragraph for lack of written description is therefore respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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